Gynecologic Oncology Reports 2 (2012) 92–93

Contents lists available at SciVerse ScienceDirect

Gynecologic Oncology Reports

journal homepage: www.elsevier.com/locate/gynor

Case Report

Topical treatment of recurrent vaginal melanoma in situ with imiquimod: A case report

Lauren S. Prescott [a], Nicholas E. Papadopoulos [b], Elizabeth D. Euscher [c], Jack L. Watkins [d], Kathleen M. Schmeler [e,*]

[a] Department of Obstetrics and Gynecology, Dartmouth-Hitchcock Medical Center, NH, USA
[b] Department of Melanoma Medical Oncology, The University of Texas MD Anderson Cancer Center, TX, USA
[c] Department of Pathology, The University of Texas MD Anderson Cancer Center, TX, USA
[d] Department of Pharmacy, The University of Texas MD Anderson Cancer Center, TX, USA
[e] Department of Gynecologic Oncology, The University of Texas MD Anderson Cancer Center, TX, USA

ARTICLE INFO

Article history:
Received 12 March 2012
Accepted 22 April 2012
Available online 30 April 2012

Keywords:
Melanoma
Imiquimod
Melanoma-in-situ
Vaginal neoplasm
Vulvar neoplasm

Introduction

Vaginal melanoma is a rare disease with an overall poor prognosis. Surgical excision is currently the modality of choice in patients with localized disease [1]. There is a paucity of data regarding the use of topical agents for the management of vaginal melanoma and melanoma in situ. However, imiquimod cream has shown to be effective in non-gynecologic cases of lentigo melanoma with cure rates as high as 80–100% [2]. It is infrequently used in vaginal melanoma, with few reported cases in the literature. We report a case of recurrent vaginal melanoma in situ successfully treated with imiquimod.

Case report

A 68-year-old woman initially presented to her primary gynecologist in November 2009 for a routine gynecologic exam and was noted to have a left vaginal lesion near the hymenal ring. She underwent an excision of the lesion and the pathology showed malignant melanoma, mucosal lentiginous type, with Breslow thickness of 2.0 mm. The margin was positive for melanoma in situ. Positron emission tomography (PET) revealed diffuse FDG avid para-aortic and inguinal lymphadenopathy, however biopsy was negative for malignancy. The lymphadenopathy remained stable and was thought to be reactive in nature due to previous hip arthroplasty. There was no other evidence of metastatic disease.

The patient underwent a wide radical excision of the lesion with lymphatic mapping and inguinal sentinel lymph node biopsy. Her postoperative course was uncomplicated and her final pathology revealed residual melanoma in situ without invasion (Fig. 1). The left margin was focally positive for melanoma in situ. All lymph nodes were negative. The patient was observed.

Four months later, the patient was noted to have multiple areas of pigmentation on the left and right side of the vagina at the level of the hymenal ring, as well as on the right vulva. The lesions were present both in areas isolated from the previous surgical incisions as well as in the area of surgical incision. The patient underwent multiple biopsies of the lesions. Complete excision was not feasible due to the anatomic location of the lesions. Pathology revealed melanoma in-situ with no areas of invasion. Postoperatively, she was treated with imiquimod 5% cream. She applied the imiquimod to the affected area once weekly for the first month, then twice weekly for the second month, then three times weekly for the third and fourth months. Imiquimod was gradually titrated to its usual dosing for vulvar dysplasia of three times weekly in order to assess the patient's tolerance of it being applied directly in the vagina. The patient completed a total of four months of treatment with imiquimod. She tolerated the treatment with minimal burning or other side effects. Pelvic exam at the completion of treatment showed a complete response. PET scan showed stable reactive lymphadenopathy with no other evidence of disease. The patient is followed every three to four months and remains without clinical evidence of recurrent melanoma in situ or invasive melanoma 18 months after completing therapy.

Discussion

Vaginal cancer is uncommon, comprising only two to three percent of all gynecologic malignancies with vaginal melanoma as the third most common histologic type of vaginal cancer [1]. The majority

* Corresponding author at: Department of Gynecologic Oncology, Unit 1362, The University of Texas MD Anderson Cancer Center, 1515 Holcombe Blvd., Houston, TX 77030, USA. Fax: +1 713 745 7586.
E-mail address: kschmele@mdanderson.org (K.M. Schmeler).

2211-338X
doi:10.1016/j.gynor.2012.04.004

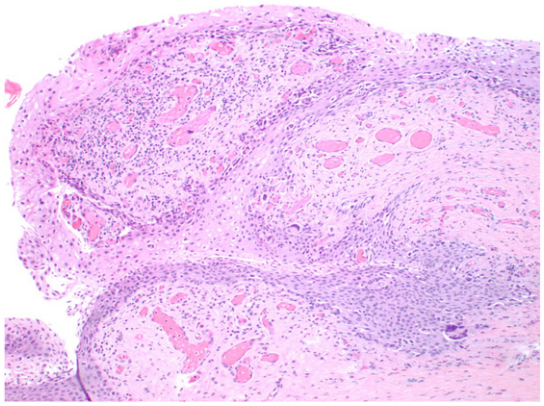

Fig. 1. Melanoma in situ: there is a diffuse proliferation of atypical epithelioid melanocytes along the basal layer (100×).

of vaginal melanomas are diagnosed at advanced stage and there is limited data on the natural history of vaginal melanoma in situ. Localized vaginal melanoma and melanoma in situ are typically treated with surgical intervention. However, for patients who are not surgical candidates or patients who have previously undergone multiple surgical resections, more conservative and less radical approaches are needed.

Tcheung et al. [3] reported 85 cases of melanoma of the female genitalia with 15 cases of primary vaginal melanoma. The majority of patients were treated with surgery, with a subset of patients also receiving immunotherapy and chemotherapy. Patients who received adjuvant therapy did not have survival differences compared to patients who were treated with surgery alone. Patients with vaginal or cervical melanoma had poorer outcomes than those with vulvar melanoma. A subsequent study by Frumovitz et al. [4] reviewed 37 cases of stage I vaginal melanoma with similar results. The majority of patients were treated with surgery, with only 10% receiving primary radiotherapy, chemotherapy or a combination of both. The median overall survival was 19 months, however patients treated with radiotherapy following wide local excision had reduced local recurrence and increased overall survival.

Imiquimod was approved by the Food and Drug Administration (FDA) for the treatment of genital warts in 1997. It has since been shown to be extremely effective in the treatment of vulvar intraepithelial neoplasia (VIN). A report by van Seters et al. [5] showed that 81% of patients with VIN treated with imiquimod had at least a 25% reduction in the size of their lesion. Furthermore, 58% of patients cleared the HPV virus after sixteen weeks of treatment. Imiquimod has also been used to treat many skin conditions and dermatologic malignancies, including basal cell carcinoma and non-gynecological melanoma [6]. Imiquimod is a topical immune-modulating agent that stimulates synthesis and release of pro-inflammatory cytokines such as interferon-alpha, interleukin-12 and tumor necrosis factor-alpha [2]. It stimulates up regulation of antiviral and antitumor activity and thus when applied to pre-malignant or malignant lesions leads to infiltration of immune cells, resulting in its antitumor effects. In a case series of 32 patients with facial lentigo maligna treated with daily imiquimod, 100% were found to have a complete response. One patient recurred 30 months after completing treatment [7].

There are limited data regarding the use of imiquimod for the treatment of vulvar and vaginal melanoma in situ [8,9]. Lonsdale-Eccles and colleagues [8] reported on a 68-year-old patient who had experienced multiple recurrences of vulvar melanoma in situ. After numerous surgeries, she elected for topical treatment with imiquimod. She was treated for four months with a complete clinical response, and is without evidence of disease 18 months following treatment [8]. Sadownik et al. [9] described a 72-year-old patient with recurrent melanoma in situ of the vulva who was treated post operatively with imiqiuimod. She was treated for six weeks following a wide local excision with positive margins with complete clinical and histological regression. She remains without evidence of recurrent disease 10 months after completing treatment [9]. Similarly, Smyth et al. [10] reported on two patients with locally recurrent vaginal mucosal melanoma treated with imiquimod. The first patient had a near complete resolution and the second patient remains disease free ten years after her original diagnosis.

In summary, we report a case of recurrent vaginal melanoma in situ successfully treated with imiquimod. The treatment was well tolerated and may prove to be a useful adjunct for patients with vulvar or vaginal melanoma in situ. Treatment with imiquimod may avoid the disfigurement, pain and postoperative complications potentially associated with repeated surgical intervention for vulvar or vaginal melanoma in situ.

Informed consent

Informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the consent is available for review by the Editor-in-Chief of this journal upon request.

Conflict of interest statement

The authors have no conflicts of interest to declare.

References

Berek, J.S., Hacker, N.F., 1994]. Practical Gynecologic Oncology, 2nd ed. Williams & Wilkins, Baltimore, pp. 576–586.

Narayan, R., Nguyen, H., Bentow, J.J., Moy, L., Lee, D.K., Greger, S., Haskell, J., Vanchinathan, V., Chang, P.L., Tsui, S., Konishi, T., Comin-Anduix, B., Dauphine, C., Vargas, H.I., Economou, J.S., Ribas, A., Bruhn, K.W., Craft, N., 2012]. Immunomodulation by imiquimod in patients with high-risk primary melanoma. J. Invest. Dermatol. 132, 163–169.

Tcheung, W.J., Selim, M.A., Herndon II, J.E., Abernethy, A.P., Nelson, K.C., 2012]. Clinicopathologic study of 85 cases of melanoma of the female genitalia. J. Am. Acad. Dermatol.

Frumovitz, M., Etchepareborda, M., Sun, C.C., Soliman, P.T., Eifel, P.J., Levenback, C.F., Ramirez, P.T., 2010]. Primary malignant melanoma of the vagina. Obstet. Gynecol. 116, 1358–1365.

van Seters, M., van Beurden, M., ten Kate, F.J., Beckmann, I., Ewing, P.C., Eijkemans, M.J., Kagie, M.J., Meijer, C.J., Aaronson, N.K., Kleinjan, A., Heijmans-Antonissen, C., Zijlstra, F.J., Burger, M.P., Helmerhorst, T.J., 2008]. Treatment of vulvar intraepithelial neoplasia with topical imiquimod. N. Engl. J. Med. 358, 1465–1473.

Cotter, M.A., McKenna, J.K., Bowen, G.M., 2008]. Treatment of lentigo maligna with imiquimod before staged excision. Dermatol. Surg. 34, 147–151.

Buettiker, U.V., Yawalkar, N.Y., Braathen, L.R., Hunger, R.E., 2008]. Imiquimod treatment of lentigo maligna: an open-label study of 34 primary lesions in 32 patients. Arch. Dermatol. 144, 943–945.

Lonsdale-Eccles, A.A., Morgan, J.M., Nagarajan, S., Cruickshank, D.J., 2006]. Successful treatment of vulval melanoma in situ with topical 5% imiquimod cream. Br. J. Dermatol. 155, 215–217.

Sadownik, L.A., Crawford, R.I., 2010]. Post-surgical treatment of melanoma in situ of the vulva with imiquimod. J. Obstet. Gynaecol. Can. 32, 771–774.

Smyth, E.C., Flavin, M., Pulitzer, M.P., Gardner, G.J., Costantino, P.D., Chi, D.S., Bogatch, K., Chapman, P.B., Wolchok, J.D., Schwartz, G.K., Carvajal, R.D., 2011]. Treatment of locally recurrent mucosal melanoma with topical imiquimod. J. Clin. Oncol. 29, e809.